Draft Panel Questions

1. Preclinical animal evaluations included in this PMA have shown that the rate and amount of DMSO can cause vasospasm and vascular wall damage. Patients undergoing staged embolization procedures for Cerebral Arteriovenous Malformations will be exposed repeatedly to DMSO since they will undergo procedures over a period of time prior to resection. Do you believe that the data in the PMA adequately support the safety of repeated exposure to DMSO as required in the proposed use of the product? If not, please provide suggestions on the additional preclinical studies that you believe are needed to demonstrate the safety of the repeated exposure to DMSO.

2. 21 CFR 860.7(d)(1) states that there is a reasonable assurance that a device is safe when it can be determined that the probable benefits to health from use of the device for its intended uses, when accompanied by adequate instructions for use and warnings against unsafe use, outweigh any probable risks. Please discuss whether the data in the PMA for Onyx Liquid Embolic System provide a reasonable assurance of safety.

3. 21 CFR 860.7(e)(1) states that there is a reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warning against unsafe use, will provide clinically significant results. Please discuss whether the data in the PMA for the Onyx Liquid Embolic System provide a reasonable assurance of effectiveness.

4. A number of complications were observed in the study that appear to relate to user training. Of particular concern were the device-related complications of difficulty in removing the catheter (10–Onyx, 0–nBCA), catheter shaft rupture (2–Onyx, 0–nBCA) and poor penetration/visualization (5–Onyx, 0–nBCA). Please comment on the sponsor's proposed training plan and whether you believe it is adequate to help ensure proper device use.

5. The device is intended for presurgical embolization and therefore, the material is meant to be removed during surgical resection of the AVM. Although patients were enrolled in this study based upon the criterion that they were surgical candidates, in some cases, the clinical course of treatment changed such that some subjects did not undergo surgical excision, post-embolization. Considering that it is probable that this scenario will also arise under clinical use, if you recommend approval, do you believe a long-term follow-up study for patients not undergoing surgical resection of their AVM should be conducted as a post-approval commitment?